UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,041	12/26/2001	Luc Desnoyers	P3030R1C8	4333

7590 03/20/2003

Ginger R. Dreger
Knobbe Martens Olson & Bear
201 California Street, Suite 1150
San Francisco, CA 94111

EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	8

DATE MAILED: 03/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,041	DESNOYERS ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/26/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's preliminary amendment filed on 26 December 2001 is acknowledged and entered. Following the amendment, the original claims 1-21 are canceled, and the new claims 22-41 are added.

Currently, claims 22-41 are pending and under consideration.

Formal Matters:

Priority

This application claims priority to US provisional application 60/115,552, PCT/US00/05601, and US application 09/931,836 (see paper No. 5). For the following reasons, the Examiner finds that the present claims 22-41 are not supported in the manner required by 35 U.S.C. 101 and 112, first paragraph by all of the prior applications, thus the present claims are not entitled to the benefit of the filling date of all of the prior applications.

The priority application 60/115,552, filed on 12 January 1999, merely discloses the nucleic acid sequence of SEQ ID NO:1 encoding PRO1484 polypeptide, and the amino acid sequence of PRO1484 (SEQ ID NO:2), and indicates that the polypeptide has homology to adipocyte complement-related protein. The prior application 60/115,552 fails to provide any specific, substantial and credible utility for the claimed PRO1484 polypeptide, and provides no guidance or working examples to teach how to used the claimed invention. Therefore, the Examiner is not able to establish that the priority document 60/115,552 satisfies the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph. As such, the claims of the instant application are not entitled to the benefit of the filling date of prior application 60/115,552. Priority is granted to the filing date of the later application, PCT/US00/05601, filed on 01 March 2000, wherein some specific and substantial biological properties of said PRO1484 polypeptide were disclosed, such as inducing re-differentiation of chondrocytes (Example 36).

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Claims

Applicant's attention is directed to 37 CFR 1.821. (d), which reads as follows:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Claims 22-33 and 35 are objected to under 37 CFR 1.821. (d) for identifying a nucleotide sequence by a figure with SEQ ID NO: in parenthesis. The correct format to define a sequence structure is by referring to its SEQ ID NO. Correction is required.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-27, 30, 31, and 35 recite the "extracellular domain". However, the protein identified as PRO1484 is a soluble protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises the "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such domains, and the specification does not define such. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain ..., lacking its associated signal sequence" (claim 22, parts (c) and (d), for example) is indefinite as a signal sequence is not generally considered to be

part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

Claim 36 is indefinite because the claims are incomplete for omitting essential elements. The claim is limited by a hybridization method "under stringent conditions". The specification does not define such conditions. As the target sequence is specific, an artisan needs to know the specific corresponding hybridization conditions in order to practice the claimed invention. The claim recites neither hybridization conditions to ensure that any hybridized polynucleotides will comprise specific sequence within the meaning of the disclosure, nor process steps which would effect the removal of nonspecific hybridization complexes. Without knowing what conditions are comprised by "stringent" conditions, one can not determine the metes and bounds of nucleic acids within the limitations of the claim.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-27, 30, 31, and 35-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a nucleic acid of SEQ ID NO:1, and a nucleic acid encoding a polypeptide of SEQ ID NO:2, does not reasonably provide enablement for claims to various variants and fragments of SEQ ID NO:1 or of a nucleotide sequence encoding SEQ ID NO:2, which do not have a functional activity, or do not have the same functional activity as SEQ ID NO:2, such as % variants (claims 22-26 and 38-41, for example), hybridization variants thereof (claim 35 and 36, for example), fragments of hybridization variants (claim 37, for example), a fragment encoding the extracellular domain SEQ ID NO:2 (claims 30 and 31, for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited

to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to % variants, hybridization variants, and fragments of the nucleic acid of SEQ ID NO:1, or of a nucleic acid encoding a polypeptide of SEQ ID NO:2, or the extracellular domain thereof, which read on any or all variants meeting the sequence limitation, and encoding polypeptides either with or without a functional activity. The claims encompass an unreasonable number of nucleic acids encoding inoperative polypeptides. However, while the specification teaches that PRO1484 polypeptide of SEQ ID NO:2 is capable of inducing re-differentiation of chondrocytes (Example 36), it provides no guidance or working examples as to how the skilled artisan could use a nucleic acid encoding an inactive polypeptide variant or fragment of SEQ ID NO:2, as no functional limitation associated with the variants in the claims. The working example, Example 37, is noted, which indicates that PRO1484 polypeptide of SEQ ID NO:2 is capable of *affecting* glucose or FFA uptake by skeletal muscle cells. However, such example cannot be used to support enablement issue of the invention as "affecting" does not clearly specify the functional property PRO1484 possesses, and the specification teaches that it could be either stimulating or inhibiting glucose or FFA uptake. As such, one of skilled in the art would not know how to use the claimed invention based upon that example.

With respect to the fragment of "the extracellular domain", the specification indicates PRO1484 is a secreted protein, and does not define such domain, therefore, it is unclear whether such domain exists, and what kind of functional property it may possess. The specification provides no guidance or working example as to how to make and use such a fragment.

Further, with respect to the hybridization variants of said nucleotides, the claims read on any or all nucleotides hybridizing to SEQ ID NO:1 or to those encoding SEQ ID NO:2. It is well known in the art that hybridization will occur even under stringent conditions if there is only local identity between two molecules whose sequences might be totally divergent outside of that region. Such hybridized molecules may encode proteins capable of inducing re-differentiation of chondrocytes, yet have other distinct biological functions from those of SEQ ID NO:2. The

specification does not define a specific hybridization condition for obtaining the claimed species, or working examples of any such variants, which would be within the limitations of the claims. Therefore, it would require undue experimentation in order to make the claimed invention in its full scope.

Furthermore, with respect to the small nucleotide fragment of 10 nucleotides of said hybridization variant, it may comprise 10 nucleotides which have no sequence homology to SEQ ID NO:1 or to those encoding SEQ ID NO:2. The specification provides no instruction, guidance, or working example regarding such fragments. Clearly, one of skill in the art would not know how to use such a fragment, it would require undue experimentation to practice the invention in a manner commensurate in scope with the claims.

Due to the large quantity of experimentation necessary to determine how to use the nucleic acids encoding inoperative polypeptides, and the small fragments thereof, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which embrace a broad class of structurally diverse variants and fragments, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 22-27, 30, 31, and 35-37 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a nucleic acid having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, SEQ ID NO:1 (claims 22-26), or a nucleic acid encoding a polypeptide of SEQ ID NO:2 (claims 22-26, for example), hybridization variants thereof under stringent conditions (claims 35 and 36), fragments of the hybridization variants (claim 37), a fragment encoding the extracellular domain SEQ ID NO:2 (claims 30 and 31, for example). The claims do not require that the encoded polypeptides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing

feature. Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In the instant application, applicants have a single polypeptide with a specific function that has not been correlated to any particular structural regions. Therefore, only isolated nucleic acids encoding the amino acid sequence set forth in SEQ ID NO:2, but not the full

breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. This is particularly important in absence of a specific known activity. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following rejections under 35 U.S.C. §§ 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 01 March 2000, which is the filing date of the application of PCT/US00/05601.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 22-27, 30, 31 and 35-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Dumas et al., WO 99/06551-A2.

Dumas discloses a nucleic acid sequence, SEQ ID NO:149, which comprises nucleotides 1-449 of SEQ ID NO:1 of the instant invention with 100% sequence identity, and encodes a human secreted protein having an amino acid sequence of SEQ ID NO:307, and comprising amino acids 1-124 of SEQ ID NO:2 of the instant invention with 100% sequence identity (see computer printout of the search results). The cited nucleotide sequence, therefore, anticipates claims 22-27, 30, 31, 35-37 as being a nucleic acid having at least 99% sequence identity to a nucleic acid sequence encoding the extracellular domain of the polypeptide of SEQ ID NO:2 (as part (c) of claims 22-27, for example), or being a nucleic acid hybridizing to a nucleic acid encoding the extracellular domain of the polypeptide of SEQ ID NO:2 (as claims 35-37).

Further, Dumas teaches an expression vector comprising the nucleic acid encoding the protein, and a host cell thereof, wherein the nucleic acid encoding the protein to be expressed is operably linked to control sequences, such as a promoter, and the expression vector may be any of mammalian, *yeast*, insect or bacterial expression systems known in the art (the paragraph bridging pages 11 and 12, and Example 30). The reference, therefore, also anticipates claims 38-41.

Claims 22-25 and 35-41 are rejected under 35 U.S.C. 102(a) as being anticipated by Strachan et al., WO 99/55865-A1.

Strachan discloses a polynucleotide sequence, SEQ ID NO:203, which encodes a rat skin cell protein (SEQ ID NO:280), and comprises a nucleotide sequence having 96% sequence similarity to a nucleic acid sequence encoding SEQ ID NO:2 of the present invention (see computer printout of the search results). The cited sequence, therefore, anticipates claims 22-25 and 35-37 as being a nucleic acid having at least 95% sequence identity to a nucleic acid sequence encoding the polypeptide of SEQ ID NO:2, or a nucleic acid hybridizing to a nucleic acid sequence encoding the polypeptide of SEQ ID NO:2 under stringent conditions. Additionally, Strachan teaches an expression vector comprising said polynucleotide, a host cell thereof (page 3, lines 6-8 and 27-29, and claims 1-3), and preferred host cells such as E.coli, yeast, and CHO (page 7, lines 25-27). Thus, the reference also anticipates claims 38-41.

Claims 22-25 and 35-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Strachan, US 6,150,502, for the same reason above as the pertained disclosure in the patent is identical to that in WO 99/55865-A1.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
3/5/03